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## NOTICE OF ALLOWANCE AND FEE(S) DUE

65482 7590 01/12/2009

INVITROGEN CORPORATION  
C/O INTELLEVATE  
P.O. BOX 52050  
MINNEAPOLIS, MN 55402

EXAMINER

STAPLES, MARK

ART UNIT

PAPER NUMBER

1637

DATE MAILED: 01/12/2009

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,594	06/22/2000	Irina Nazarenko	IVGN 246	8750

TITLE OF INVENTION: PRIMERS AND METHODS FOR THE DETECTION AND DISCRIMINATION OF NUCLEIC ACIDS

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$0	\$0	\$1510	04/13/2009

**THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.**

**THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.**

### HOW TO REPLY TO THIS NOTICE:

#### I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

**IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.**

# **PART B - FEE(S) TRANSMITTAL**

**Complete and send this form, together with applicable fee(s), to: Mail Mail Stop ISSUE FEE  
Commissioner for Patents  
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**INSTRUCTIONS:** This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

65482 7590 01/12/2009

**INVITROGEN CORPORATION  
C/O INTELLEVATE  
P.O. BOX 52050  
MINNEAPOLIS, MN 55402**

Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

## **Certificate of Mailing or Transmission**

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

(Depositor's name)
(Signature)
(Date)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/599,594	06/22/2000	Irina Nazarenko	IVGN 246	8750

**TITLE OF INVENTION: PRIMERS AND METHODS FOR THE DETECTION AND DISCRIMINATION OF NUCLEIC ACIDS**

APPLN. TYPE	SMALL ENTITY	ISSUE FEE DUE	PUBLICATION FEE DUE	PREV. PAID ISSUE FEE	TOTAL FEE(S) DUE	DATE DUE
nonprovisional	NO	\$1510	\$0	\$0	\$1510	04/13/2009

EXAMINER	ART UNIT	CLASS-SUBCLASS
STAPLES, MARK	1637	435-006000

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

- ☐ Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
- ☐ "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list

- (1) the names of up to 3 registered patent attorneys or agents OR, alternatively, 1 \_\_\_\_\_
- (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed. 2 \_\_\_\_\_
- 3 \_\_\_\_\_

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent) : ☐ Individual ☐ Corporation or other private group entity ☐ Government

4a. The following fee(s) are submitted:

- ☐ Issue Fee
- ☐ Publication Fee (No small entity discount permitted)
- ☐ Advance Order - # of Copies \_\_\_\_\_

4b. Payment of Fee(s); (Please first reapply any previously paid issue fee shown above)

- ☐ A check is enclosed.
- ☐ Payment by credit card. Form PTO-2038 is attached.
- ☐ The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number \_\_\_\_\_ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

- ☐ a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. ☐ b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature \_\_\_\_\_

Date \_\_\_\_\_

Typed or printed name \_\_\_\_\_

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This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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EXAMINER

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## Determination of Patent Term Adjustment under 35 U.S.C. 154 (b) (application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 0 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 0 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

<b>Notice of Allowability</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/599,594	NAZARENKO ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Mark Staples	1637	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 09/29/2008.
2. ☒ The allowed claim(s) is/are 11, 12, 14, 15, 17-19, 59, and 63-67.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) ☐ All    b) ☐ Some\*    c) ☐ None    of the:
    1. ☐ Certified copies of the priority documents have been received.
    2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
  - \* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1) ☐ hereto or 2) ☐ to Paper No./Mail Date \_\_\_\_\_.
  - (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

**Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).**
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

**Attachment(s)**

- |  |  |
|--|--|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892)   | 5. <input type="checkbox"/> Notice of Informal Patent Application                      |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 6. <input type="checkbox"/> Interview Summary (PTO-413),<br>Paper No./Mail Date _____. |
| 3. <input checked="" type="checkbox"/> Information Disclosure Statements (PTO/SB/08),<br>Paper No./Mail Date <u>03/17/2003</u> | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment                    |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit<br>of Biological Material                     | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance   |
|  | 9. <input type="checkbox"/> Other _____.   |

/Kenneth R Horlick/  
Primary Examiner, Art Unit 1637

### **DETAILED ACTION**

1. Applicant's amendment of claims 11, 12, and 18 and the cancellation of claims 78 and 79 in the paper filed on 09/29/2008 is acknowledged.

Claims 11, 12, 14, 15, 17-19, 59, and 63-67 are pending and at issue.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### **EXAMINER'S AMENDMENT**

2. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Attorney Perfect on 12/23/2008. Applicant is advised to carefully review the amendments, especially the chemical names, for accuracy as supported by the originally filed specification.

Claims 11, 12, and 18 are amended as follows. Please note that in claim 18 the comma is deleted which follows "ROX (6-carboxy-X-rhodamine)" and which is prior to the semi colon.

11. (Currently amended) A method for the quantitation or detection of one or more target nucleic acid molecules in a sample during nucleic acid synthesis comprising:

mixing one or more a target nucleic acid molecules with one or more fluorescently labeled oligonucleotides, wherein said one or more oligonucleotides are labeled with only a single type of fluorescent label ~~, said single type of fluorescent label having the same chemical structure,~~ and said oligonucleotide undergoes a detectable change in fluorescence upon hybridization of said one or more oligonucleotides to said one or more target nucleic acid molecules;

incubating said mixture under conditions sufficient to synthesize one or more nucleic acid molecules complementary to all or a portion of said one or more target nucleic acid molecules, said one or more synthesized nucleic acid molecules comprising said one or more oligonucleotides; and

detecting the presence or absence or quantifying the amount of said one or more synthesized nucleic acid molecules by measuring said fluorescent label; wherein said fluorescent label is selected from the group consisting of JOE (2'7'-dimethoxy-4'5'-dichloro-6-carboxyfluorescein), FAM (5-carboxyfluorescein), TAMRA (N,N,N',N'-tetramethyl-6-carboxyrhodamine), or ROX (6-carboxy-X-rhodamine).

12. (Currently amended) A method for quantitation or detection of one or more target nucleic acid molecules in a sample during nucleic acid amplification comprising:

mixing one or more target nucleic acid molecules with one or more fluorescently labeled oligonucleotides under conditions sufficient to amplify one or more nucleic acid molecules complementary to all or a portion of said one or more target nucleic acid molecules, said one or more amplified nucleic acid molecules comprising said one or more oligonucleotides, wherein said one or more oligonucleotides are labeled with only a single type of fluorescent label ~~, said single type of fluorescent label having the same chemical structure,~~ and said oligonucleotide undergoes a detectable change in fluorescence upon hybridization of said one or more oligonucleotides to said one or more target nucleic acid molecules; and

detecting the presence or absence or quantifying the amount of said one or more target nucleic acid molecules by measuring said fluorescent label; wherein said fluorescent label is selected from the group consisting of (2'7'-dimethoxy-4'5'-dichloro-6-carboxyfluorescein), FAM (5-carboxyfluorescein), TAMRA (N,N,N',N'-tetramethyl-6-carboxyrhodamine), or ROX (6-carboxy-X-rhodamine).

18. (Currently amended) A method for amplifying a double stranded nucleic acid molecule, comprising:

providing a first and second primer, wherein said first primer is complementary to a sequence within or at or near the 3"-termini of the first strand of said nucleic acid molecule and said second primer is complementary to a sequence within or at or near the 3"-termini of the second strand of said nucleic acid molecule;

hybridizing said first primer to said first strand and said second primer to said second strand in the presence of one or more polymerases, under conditions such that said primers are extended to result in the synthesis of a third nucleic acid molecule complementary to all or a portion of said first strand and a fourth nucleic acid molecule complementary to all or a portion said second strand;

denaturing said first and third strands, and said second and fourth strands; and

repeating the above steps one or more times, wherein one or both of said first and second primers are labeled with only a single type of fluorescent label, ~~said single type of fluorescent label having the same chemical structure~~; wherein said fluorescent label is selected from the group consisting of (2'7'-dimethoxy-4'5'-dichloro-6-carboxyfluorescein), FAM (5-carboxyfluorescein), TAMRA (N,N,N',N'-tetramethyl-6-carboxyrhodamine), or ROX (6-carboxy-X-rhodamine);

and wherein said primer undergoes a detectable change in fluorescence upon hybridization of said one or more labeled primers to said nucleic acid molecule.

**Objections and Rejections that are Withdrawn/ Moot**

***Canceled Claim Rejections Moot / Withdrawn***

3. The objection to cancelled claims 78 and 79 is moot and therefore is withdrawn.

***Claim Rejections Withdrawn - 35 USC § 103***

4. The rejection of claims 11, 12, 14, 15, 17-19, 59 and 63-67 under 35 U.S.C. 103(a) as being unpatentable over Horn et al. (U.S. Patent 6,465,175) in view of Tyagi et al. (U.S. Patent 6,037,130) is withdrawn. This rejection is overcome by Applicant amending the claims to incorporate allowable subject matter and by Examiner's Amendment as given above.

**Allowable Subject Matter**

5. Claims 11, 12, 14, 15, 17-19, 59, and 63-67 are allowed.
6. The following is a statement of reasons for the indication of allowable subject matter: in the absence of any evidence, the ordinary practitioner would expect that all fluorescent labels would function equally well in the claimed assay. The closest prior art found was Horn et al. (U.S. Patent 6,037,130). However, Horn specifically teaches that "Extensive quenching was observed with the BODIPY FL-labeled oligomer, in contrast to the fluorescein- and Texas Red-labeled oligomers which did not show noticeable quenching under the same hybridization conditions (see column 14, lines 23- 27)." In contrast, Applicant's specification expressly shows that each of the claimed labels, including fluorescein and rhodamine, function in the assay. Given direct experimental evidence demonstrated by Applicant, opposed by just a negative teaching of Horn that

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is not supported by data, the claims are found to be enabled. However, the negative teaching by Horn qualifies under M.P.E.P. 2145 as a direct teaching away from the use of the labels required in the claims. Consequently, there is no case of *prima facie* obviousness due to the express teaching away of the Horn reference for use of fluorescein- and Texas-red- type labels, and no reasonable expectation that such labels would therefore function in the claimed assay. For these reasons, the indicated claims reciting the specific labels, are allowed.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark Staples whose telephone number is (571) 272-9053. The examiner can normally be reached on Monday through Thursday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1637

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Mark Staples

/M. S./

Examiner, Art Unit 1637

January 3, 2009

/Kenneth R Horlick/

Primary Examiner, Art Unit 1637